REMARKS

Applicants respectfully maintain that the present Amendment is timely filed in view of October 10, 2009 falling on a Saturday and Monday October 12, 2009 being a federal holiday.

Claims 35-52 and 63-64 have been examined. Claims 57-61 have been cancelled without prejudice in response to the finality of the requirement for restriction. Claim 35 has been amended to specify that the binding region referred to on the third line is that of the second peptide, for better clarity. In addition the reference to Tat and gp120 has been included next to the relevant sequence identifiers, again for improved clarity. Claim 38 has been amended to specify that Tat is native Tat. This is supported by the as-filed Specification at page 19, line 3.

Claim 36 has been amended to delete the recitation of a reference. Claims 37-52, 63 and 64 have been amended to correct inadvertent errors in dependency, and claims 49 and 51 have been amended to recite proper Markush language.

None of the amendments made herein constitutes the addition of new matter.

The Requirement for Restriction

The Patent Office has made the requirement for restriction under 35 U.S.C. 121 and 372 final.

In response to the finality of the restriction requirement, Applicants have cancelled claims 56-60. In anticipation of allowance of the claims of Group I, the remaining claims are maintained in the application for the present.

The Objections to the Claims

Claims 37-52, 63, and 64 have been objected to due to depending from a cancelled claim. In the interest of advancing prosecution, claims 37-52, 63, and 64 have been amended to obviate this objection.

Claims 49 and 51 were objected to for improper Markush language. In the interest of advancing prosecution, claims 49 and 51 have been amended to obviate this objection.

The Invention

Applicants respectfully provide the following discussion of the claimed invention to facilitate the discussion of the rejections and to make clear the basis of the invention as claimed.

The present invention relates to the discovery that Tat binds to Env/gp120, which can only occur when the V3 loop is exposed. From this discovery flows the use of a Tat-gp120 complex for use an immunogen and in immunogenic compositions and methods. Consistent with the novelty of the present invention, the last paragraph of page 22 of the Specification discusses new B cell epitopic determinants for the Tat/Env complex, formed via the V3 loop.

The Rejections under 35 U.S.C. 112, first paragraph

Claims 35, 37-52, 63 and 64 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the requirement for written description. Applicants respectfully traverse this rejection.

The Patent Office has said that the rejection was made because the claims are interpreted as being drawn to a genus of peptides recited as fragment, mutants or variants thereof. The Patent Office has concluded that there is insufficient recitation of distinguishing identifying characteristics.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claim 35 to specify the functional activity of the fragment, mutant or variant. Applicants note that the first peptide comprises the V3 loop of gp120, and the second peptide comprises the region of Tat that binds the V3 loop, or analogs of Tat that can bind the V3 loop. The Specification provides support for specific binding between the two peptides, at page 5, third paragraph. Although the discussion of this paragraph is in relation to the association or dissociation of the

two peptides, it is clear than binding is preferred. Furthermore, the numerous references throughout the Specification make it clear that the two peptides can bind, i.e., are "capable of binding." In addition the fragment, mutant or variant of Tat capable of binding gp120 is further defined such that capable of binding a region on gp120 comprising the particular recited residues. As is clear, residues 301-419 is the region of gp120 containing the V3 loop (see fourth paragraph on page 7) particularly when taken in combination with the last paragraph on page 6, which describes that SEQ ID NO:2 is the sequence of gp120, gp120 being well-known as part of Env. Thus, there is both structural and functional language in the claims which clearly establish that the inventors possessed the invention as of the filing date of this application.

Claim 36 has been amended in a similar fashion to that of claim 35 in respect of the clarification of the binding region of the second peptide and the binding between the first and second peptides. In addition, reference to "the" monoclonal antibody has been rewritten as "a" monoclonal antibody.

Claim 38 has been amended to specify that Tat is native Tat. This is supported by the as-filed Specification at page 19, line 3.

Applicants respectfully maintain that one of ordinary skill in the art, reading the claims and the instant Specification, understands that the inventors were in full possession of the invention as claims. In view of the foregoing discussion and the amendments to the claims, Applicants respectfully maintain that the requirements of the statute are met, it is clear to the skilled artisan that the inventors were in possession of the invention as claimed at the time the application was filed, and the rejection should be withdrawn.

The Rejections under 35 U.S.C. 112, second paragraph

Claims 35, 37-52, 63 and 64 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

The Patent Office has alleged that the recitation of fragment, mutant or variant thereof renders the claims indefinite because "one would not know what type of fragment, mutant or variant thereof would be immunogenic or capable of binding the specified residues of SEQ ID NO:1 or 2."

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claims 35 and others to specify the functional activity of the fragment, mutant or variant and to recite particular amino acids associated with the ability of the two peptides to bind specifically with one another.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended claim 35 to specify the functional activity of the fragment, mutant or variant. Applicants note that the first peptide comprises the V3 loop of gp120, and the second peptide comprises the region of Tat that binds the V3 loop, or analogs of Tat that can bind the V3 loop. The Specification provides support for specific binding between the two peptides, at page 5, third paragraph. Although the discussion of this paragraph is in relation to the association or dissociation of the two peptides, it is clear than binding is preferred. Furthermore, the numerous references throughout the Specification make it clear that the two peptides can bind, i.e., are "capable of binding." In addition the fragment, mutant or variant of Tat capable of binding gp120 is further defined such that capable of binding a region on gp120 comprising residues… As is clear, residues 301-419 is the region of gp120 containing the V3 loop (see fourth paragraph on page 7) particularly when taken in combination with the last paragraph on page 6, which describes that SEQ ID NO:2 is the sequence of gp120, gp120 being well-known as part of Env. It is believed that this is resolves the rejection.

Claim 36 is allegedly indefinite for incorporation of information from a reference.

In the interest of advancing prosecution and without acquiescing to the rejection, claim 36 has been amended to delete the incorporation of the reference.

In view of discussion in the present response and with the amendments to

claims to better claim the invention, Applicants respectfully maintain on the record that the claims are sufficiently clear and definite as to fulfill the statutory requirements, particularly in the eyes of the skilled artisan reader of the present application. Accordingly, the rejection under 35 U.S.C. 112, second paragraph, should be withdrawn.

The Rejections under 35 U.S.C. 102

Claims 35-40, 42, 45, 50-51, 63 and 64 have been rejected under 35 U.S.C. 102(b) as allegedly unpatentable over Voss et al. (WO 01/54719). Applicants respectfully traverse this rejection.

Traverse is made below the listing of all the Section 102 rejections.

Claims 35-40, 42, 45, 50-51, and 63 have been rejected under 35 U.S.C. 102(b) as allegedly unpatentable over Voss et al. (2003) J. Virology 77:1049-1058. Applicants respectfully traverse this rejection.

Claims 35-42, 45, 50-52, 63 and 64 have been rejected under 35 U.S.C. 102(b) as allegedly unpatentable over Debrus et al. (WO 02/087614). Applicants respectfully traverse this rejection.

Applicants respectfully note that SEQ ID NO:1 is the Tat sequence, while SEQ ID NO:2 is the gp120 sequence. Thus, the main claim can be paraphrased to equate to the gp120 loop bound to the appropriately specified region of Tat. While the Specification makes several references to the Env protein, it is more accurate to refer to the gp120. Because the claims specify that the V3 loop of the first peptide is bound to the binding region of the second peptide, which can be Tat or mutants, variants or analogs thereof, the claims are not anticipated by the cited Voss reference. It is understood in the art that it is not possible for a complex between Tat and Env (gp120) to form unless a V3 loop is exposed, and this does not occur with simple mixtures of Tat and Env/gp120, as in Voss. Applicants emphasize that Voss only teaches such simple mixtures. The present Specification teaches that the V3 loop can be made available by mutation (for example in the ΔV2 mutant) or by interacting Env/gp120 with

CD4, for example. None of the cited references teaches the necessity for the accessibility of the V3 loop nor do any of the cited references teach conditions which would make the V3 loop available for binding to the Tat protein. In fact, none of the cited art recognizes that Tat mimics the CCR5 co-receptor.

The first cited Voss reference (WO) does not disclose complexes of Tat bound to the V3 loop of Env, and the conditions taught by Voss are not conducive to the formation of such complexes. In Voss, the Tat cysteines are modified to prevent the formation of disulfide bonds. This modification, in itself, prevents any interaction with the V3 loop even if the loop were exposed. Thus, this Voss reference actually teaches away from the present claimed invention. The cited Voss reference makes no teaching of the particular compositions (or methods of use) or even of their desirability. Neither does Voss appear to teach any conditions which would result in the accessibility of the V3 loop. Accordingly, the cited Voss reference cannot be properly deemed to anticipate the present claimed invention and the rejection must be withdrawn.

Applicants respectfully note that SEQ ID NO:1 is the Tat sequence, while SEQ ID NO:2 is the gp120 sequence. Thus, the main claim can be paraphrased to equate to the gp120 loop bound to the appropriately specified region of Tat. While the Specification makes several references to the Env protein, it is more accurate to refer to the gp120. Because the claims specify that the V3 loop of the first peptide is bound to the binding region of the second peptide, which can be Tat or mutants, variants or analogs thereof, the claims are not anticipated by the cited Voss reference. It is understood in the art that it is not possible for a complex between Tat and Env (gp120) to form unless a V3 loop is exposed, and this does not occur with simple mixtures of Tat and Env/gp120, as in Voss. Applicants emphasize that Voss only teaches such simple mixtures. The present Specification teaches that the V3 loop can be made available by mutation (for example in the ΔV2 mutant) or by interacting Env/gp120 with CD4, for example. None of the cited references teaches the necessity for the accessibility of the V3 loop nor do any of the cited references teach conditions which would make the V3 loop available for binding to the Tat protein. In fact, none of the cited art recognizes that Tat mimics the CCR5 co-receptor.

As relates to the cited Debrus reference, Debrus requires an HIV antigen in

conjunction with an HSV or HPV antigen. This is not the same invention as claimed. Debrus teaches no condition under which the V3 loop would be made accessible for binding. In sum, the cited Voss reference makes no teaching of the particular compositions (or methods of use) or even of their desirability. Neither does Voss appear to teach any conditions which would result in the accessibility of the V3 loop. Accordingly, the cited Debrus reference cannot be properly deemed to anticipate the present claimed invention and the rejection must be withdrawn.

The second cited Voss reference discloses different mixtures of antigens (Table 1), but there is no disclosure of any condition or treatment that would make the V3 loop of gp120 accessible for binding to any portion of the Tat protein. As above, there is no anticipation of the present claims which require the accessibility of the V3 loop for binding to the Tat protein. Thus, every feature recited in the instant claims is not present in the reference, and thus, the rejection is not proper and should be withdrawn.

In view of the foregoing, none of the cited references anticipate the claimed invention, and the three rejections for alleged anticipation must be withdrawn.

The Rejections under 35 U.S.C. 103

Claims 41, 42-44, 46-49 and 52 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Voss et al. (WO 01/54719) or Voss et al. (2003) J. Virology 77:1049-1058 as applied to claim 35 above and further in view of Gzyl et al. (2004) Virology 318:493-506, Wyatt et al. (1995) J. Virology 69:5723-5733, Sattenau et al. (1993) J. Virology 67:7383-7393, Ibrahim et al. (1999) Virus Research 60:159-169 and Watanabe et al. (2000) Vaccine 19:1199-1203. Applicants respectfully traverse this rejection.

As noted above, there is no teaching of the necessity of making the V3 loop accessible, nor is there any teaching or suggestion of conditions that would make the V3 loop accessible for binding to Tat in either of the cited Voss references. With respect to the cited Gyzl and Wyatt references, while these may disclose the advantage of various mutants of the Env/gp120 protein and the role of the V2 loop,

there is still nothing in these references to suggest that Tat mimics the CCR5 receptor or that Tat binds gp120 via the V3 loop. Gyzl and Wyatt focus on ways to improve the immunogenicity of Env and its cleavage product gp120. The cited Voss references do not teach conditions which would expose the V3 loop or otherwise allow the binding of Tat and gp120 or peptides thereof, and the Gyzl and Wyatt references are focused on Env and do not teach or suggest that the V3 loop of gp120 can bind Tat (or any advantage of such binding). Sattenau teaches that CD4 can induce the exposure of the V3 loop of gp120, but it is silent as to the binding of the exposed V3 loop to Tat. Ibrahim discusses heparin sulfate and Watanabe discusses cross-liking peptides, but neither appears to be germane to the base claims. In the absence of a motivation to expose the V3 loop as relates to binding to Tat, one of ordinary skill in the art would not have been motivated to combine these teachings to arrive at the present invention. There is no indication as to why one would have done so.

Applicants acknowledge that there is a substantial body of prior art related to HIV and potential vaccines. However, no one is believed to have identified the role of Tat as presented in the present application. Thus, there was no motivation to make the complexes or input components of the complexes, and therefore, the present invention as claimed is not obvious over the cited references.

In view of the foregoing, Applicants respectfully maintain that the present invention is not prima facie obvious over the cited references and request the withdrawal of the rejection.

Claims 43-44 and 46-49 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Debrus et al. (WO 02/087614) as applied to claim 35 above and further in view of Gzyl et al. (2004) Virology 318:493-506, Wyatt et al. (1995) J. Virology 69:5723-5733, Sattenau et al. (1993) J. Virology 67:7383-7393 and Ibrahim et al. (1999) Virus Research 60:159-169. Applicants respectfully traverse this rejection.

As a first matter, and previously discussed, the Debrus reference does not teach or suggest conditions which would make the V3 loop of gp120 accessible for

binding to Tat. In the absence of that accessibility, there can be no such binding. None of the cited references teach the binding of Tat with the V3 loop or the desirability of a complex or a V3-exposed gp120 protein or peptide. The references other than Debrus have been discussed above, and Debrus certainly does not add what those references lack, any more than do the Voss references (or vice versa).

In view of the foregoing arguments and the teachings of the Specification, for example, at page 2, where the inventors state that the binding of the V3 loop of gp120 was unexpected and the long felt need in the art for vaccines against the AIDS virus, Applicants respectfully submit that the present invention as claimed is not obvious over the cited references.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This Amendment is accompanied by a Petition for Extension of Time (three months) and a check in the amount of $1110.00 as required under 37 C.F.R. 1.17. It is believed that this amendment does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, however, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,

/donnamferber/

Donna M. Ferber
Reg. No. 33-878

GREENLEE, WINNER AND SULLIVAN, P.C.
4875 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (303) 499-8080
Facsimile: (303) 499-8089
E-mail: usptomail@greenwin.com
Attorney Docket No. 114-06
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